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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR   | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|------------------------|---------------------|------------------|
| 10/048,194      | 02/15/2002  | Michael R. Emmert-Buck | 4239-61944          | 2881             |

36218 7590 07/05/2005

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EXAMINER

HOLLERAN, ANNE L

ART UNIT PAPER NUMBER

1643

DATE MAILED: 07/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/048,194

Applicant(s)

EMMERT-BUCK, MICHAEL R.

Examiner

Anne Holleran

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-69 is/are pending in the application.
- 4a) Of the above claim(s) 45 and 55-66 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-44, 46-54 and 67-69 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-69 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 3/31/05, 6/4/04, 1/
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_

### DETAILED ACTION

1. The preliminary amendment filed 1/24/2002 is acknowledged. Claims 42-44 were amended and claims 67-69 were added.

Claims 1-69 are pending.

### *Election/Restrictions*

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-44, 46-54 and 67-69, drawn to methods of analyzing a biological specimen or a cellular specimen.

Group II, claim(s) 45, drawn to a substrate with a three dimensional matrix.

Group III, claim(s) 55-63, drawn to a device for analyzing a biological specimen, having a layered substrate.

Group IV, claim(s) 64-66, drawn to a system for molecular analysis of a biological sample, the system comprising a sample support capable of holding the sample during the movement of a component of the sample through a plurality of separation matrices.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the technical feature of group I is the use of a substrate having one or more capture regions. An example of the use of a substrate having one or more capture regions is known in the art, for example a microarray containing different hybridizing nucleic acids or different antibodies (see Schena, M. et al. Science, 270: 467-470, 1995). The technical feature of group II is that of a substrate having a three dimensional matrix. An example of such a substrate is a stack of nitrocellulose and anion-exchange membranes, which is known in the art (see Demczuk, S. et al. Proc. Natl. Acad. Sci. USA, 90 2574-2578, 1993; cited in the IDS). The technical feature of group III is that of a device containing a layered

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substrate that must include a surface to which the cellular specimen may be applied and maintained in cytoherence. The technical feature of group IV is that of a sample support capable of holding the sample during the movement of a component of the sample through a plurality of separation matrices.

Because each of the groups has a different technical feature, and because for groups I and II, the technical features are known in the art, groups I-IV lack a corresponding special technical feature that makes a contribution over the prior art as a whole.

3. During a telephone conversation with Tanya Harding on November 24, 2004 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-44, 46-54 and 67-69. Affirmation of this election must be made by applicant in replying to this Office action. Claims 45, and 55-66 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

***Claim Rejections - 35 USC § 112***

4. Claims 1-44, 49 and 67-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, from which claims 2-44 and 67-69 ultimately depends, is indefinite because there is a lack of correlation between the stated purpose of the method ("analysis of a biological specimen") and the end result of performing the steps of the method (producing "a pattern that is informative about the identification of the biological molecule").

Claim 1 is also indefinite because there is lack of antecedent basis for the phrase "the identification of the biological molecule".

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Claim 24 is indefinite because of lack of antecedent basis for "the component". In claim 1, "the components" is recited in the claims.

Claim 44 lacks antecedent basis for "the cellular specimen".

Claims 49 is indefinite because of lack of antecedent basis for "the cellular substrate".

Claim 69 lacks antecedent basis for "the cellular specimen".

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-10, 12-21, 24-30, 32-42, 44, 46-54 and 67, and 69 are rejected under 35 U.S.C. 102(a) as being anticipated by Englert (Englert, C.R. et al. Cancer Research, 60: 1526-1530, 2000, March 15; cited in the IDS).

Englert teaches methods for analyzing biological specimens such as solubilized cellular lysates and intact histological tissue sections, cryostat sections of prostate tissue. The methods of Englert include capture membranes such as nitrocellulose layers and agarose gel layers arranged in multiple layers. Englert teaches stacks of membranes of as many as 101 membranes. Englert teaches layers that are 2mm thick, and also membranes that are each less than 50µm thick. Englert teaches identification molecules that are antibodies. Englert teaches placing a specimen within a gel on the surface of a layered substrate. Englert teaches a method comprising placing

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multiple different discrete cellular specimens on the surface of the substrate (envisions 18 specimens in Figure 1). Englert teaches a cellular specimen that is a tumor specimen. Englert teaches identification of a protein such as PSA. Englert teaches identification molecules that are antibody and also cDNA-containing plasmids. Englert teaches electrical conduction of the sample through the substrate as well as capillary pressure on the specimen. Englert teaches that use of a second identification molecule for identification of a specific molecule (see PSA example, capture is polyclonal antibody and detection is monoclonal antibody). Englert teaches analysis of different specimens at different stages of tumor progression of obtaining a cell population of interest from a larger cell population (Figure 1).

Therefore, Englert teaches the methods as claimed.

6. Claims 1, 2, 42, 44, 67 and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Imai (US 5,057,438; issued Oct. 15, 1991).

Imai teaches methods of analyzing biological specimens that are antibodies or antigens by applying the specimens to a plurality of different kinds of membranes having different species of antibody or antigen on an electrophoretic carrier (see abstract).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
  2. Ascertaining the differences between the prior art and the claims at issue.
  3. Resolving the level of ordinary skill in the pertinent art.
  4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
7. Claims 1 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Englert I in view of Englert II (Englert, et al., Current Opinion in Molecular Therapeutics, 1(6): 712-719, 1999; cited in the IDS).

Englert I teaches as set forth above. Englert I fails to teach a method comprising laser capture microdissection. However, such methods are known in the art for the purpose of obtaining isolated defined cell types from a clinical sample, as evidenced by the teaches of Englert II (see page 713, second column). One would have been motivated to modify the methods of Englert I by using laser capture microdissection for the purpose of obtaining isolated defined cell types, because histological tissues can be complex, leading to complexity of the molecular analysis. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Englert I by using laser capture microdissection to further refine the analysis of a tissue section by the method of Englert I.

8. Claims 1, 43 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Englert I in view of Huang (Huang, A.-H. et al., Analytical Biochemistry, 268: 305-317, 1999).

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Englert I teaches as set forth above. Claims 1, 43 and 68 include an analysis step of using mass spectrometry to sequence a capture component for the purpose of identifying the captured component. Englert I teaches various methods for identification of captured components, but fails to explicitly teach the use of mass spectrometry. However, the use of mass spectrometry for the sequencing of proteins is known in the art. Huang teaches a method that is of use for obtaining sequence information directly from mixtures or as an adjunct of peptide mass mapping to provide protein identification. One would have been motivated to use the method of Huang for the further identification of captured proteins because Huang's method may be used on a sample that is a heterogeneous mixture. Therefore, one would have been motivated to use Huang's method, because the method of Englert I would potentially provide small amounts of captured protein that is part of gel or membrane and require further identification. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Englert I by adding to it a further step of mass spectrometry identification as taught by Huang.

### *Conclusion*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran  
Patent Examiner  
June 27, 2005

LANA M. HARRIS, PH.D.  
PRIMARY EXAMINER

